

REMARKS

Claims 1-12 are pending in the application. Claims 5, 7, 9 and 11 have been amended. Claims 13-20 have been added. Support for the new claims is found in Example 2 on page 7 of the Application. With entry of this amendment, claims 1-20 will be pending.

Claims 5-12 are rejected under 35 U.S.C. §112, first paragraph, as not being enabled. Specifically, the Examiner contends that the specification, while being enabling for the treatment of specific cancer, does not reasonably provide enablement for (1) prophylaxis of (2) a cancer illness in general. Office action, p. 2, ¶ 4. Claims 5, 7, 9 and 11 have been amended to exclude the term “prophylaxis.” Withdrawal of the §112 rejection is respectfully requested.

Claim 1 is rejected under 35 U.S.C. §103(a) as being unpatentable over Collery (WO 93/02087) in view of Hall (Anti-Cancer Drugs, 4, p. 231). According to the Examiner, “Collery et al. ... teaches that gallium(III), when complexed to N-heterocycles, shows antitumor activity,” and “Hall et al. teaches that thiosemicarbazone[,] when complexed to nickel, copper and cobalt[,] are effective at inhibiting carcinoma in vivo.” Office action, p. 9, ¶¶ 1&3. Therefore, the Examiner contends that “[o]ne would have been motivated to replace the N-heterocycles of Collery et al. with the thiosemicarbazone of Hall et al. because 1) of an expectation of success in preparing a complex with similar anti-cancerous activity in human cells to those found for various other such metal complexes of both the gallium(III) complexes of Collery et al. and of the thiosemicarbazone-metal complexes of Hall et al. and 2) because Hall et al. teaches that by switching the metal portion of the complexes taught therein, a different magnitude of cancer inhibition can be achieved.” Office action, p. 10, ¶ 2.

In order for the Examiner to establish a *prima facie* case of obviousness: 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the teachings; 2) there must be a reasonable expectation of success; and 3) the references must teach or suggest all of the claimed limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on the Applicant’s disclosure. *In Vaeck*, 947 F.2d 422, 20 USPQ2d 1438 (Fed. Cir. 1991).

The Applicant respectfully traverses the rejection because the Examiner has failed to establish a *prima facie* case of obviousness for the reasons set forth below.

Hall discloses the cytotoxicity of heterocyclic thiosemicarbazones and their metal complexes on human and murine tissue culture cells. Specifically, Hall discloses an octahedral nickel(II) complex, (Ni[L4DE]₂), wherein the nickel is complexed by a pair of 2-acetylpyridine-4,4-diethyl thiosemicarbazone ligands. Hall, p. 232 (compound #4). The cytotoxicity of this compound against human colon adenocarcinoma and murine leukemia silanes is summarized in Table 2.

Hall does not disclose any charged complexes but, quite to the contrary, only discloses an uncharged transition metal complex. In contrast, independent claim 1 recites a charged complex comprising gallium. Gallium is a main group metal. Generally, main group metals exhibit chemical behavior different from transition metals. Further, the activities of the claimed compounds are significantly higher than those of compound #4 in Hall, as can be seen by comparing the Applicant's IC₅₀ values in Example 2 (see Application, p. 7) with Hall's ED₅₀ values in Table 2 (see Hall, p. 234). The Applicant's IC₅₀ value and Hall's ED₅₀ value define the same activities, namely, the concentration that is necessary to reduce the cell growth by 50% (see, also Hall, p. 233, left column, lines 9-10).

Collery teaches gallium(III) complexes with different ligands as compared to the complexes of the present claims (see Collery, p. 2, lines 3-35). Moreover, Collery et al. teaches the use of complexes of formula (VI) as pharmaceutical agents having antiviral and antitumoral activities, in which the ligands may be 8-hydroxy-quinoline (see Collery, p. 4, lines 4-20). Thus, Collery's ligands of the gallium(III) complexes are chemically significantly different from Hall's ligands of the transition metal complexes. Accordingly, a person skilled in the art would not be motivated based on the disclosure of either of these documents, to select one specific metal atom, namely gallium, and choose the ligands according to Hall.

Additionally, the Applicant notes that the Examiner's obviousness rejection, based on Collery and Hall, seems to contradict the reasoning of non-enablement. As support for the non-enablement rejection, the Examiner contends that "different thiosemicarbazone compounds have been shown to have significantly different results in their treatment of cancer." Office action, p. 7, ¶ 2. "Accordingly, the effectiveness of any given compound of the instant invention would need to be determined individually." *Id.* These statements seem to refute the contention that combining Hall's ligands with Collery's metal to produce a compound having the tumor-inhibiting activity would be obvious. In other words, if the art is so unpredictable, as the

Examiner contends, then it would not be obvious to one skilled in the art to replace the ligands of Collery's complexes with the ligands of Hall's complexes, which have a completely different metal atom.

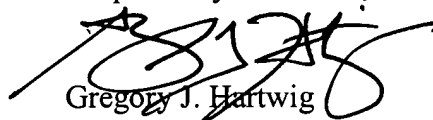
In conclusion, and as discussed above, it has been surprisingly found the claimed compounds are highly active for treating cancer diseases. Nothing in Hall or Collery suggests changing or exchanging a metal atom.

Therefore, independent claim 1 and its dependent claims 2-20 are allowable. Reconsideration and allowance of independent claim 1 and corresponding dependent claims 2-12, and consideration and allowance of dependent claims 13-20 are respectfully requested. In addition, dependent claims 2-20 may contain additional patentable subject matter, which may or may not be discussed herein.

In view of the foregoing, the application is in condition for allowance. Reconsideration and allowance of the application are respectfully requested. Should any issues remain precluding allowance of the application, the Examiner is strongly encouraged to contact the undersigned at the telephone number listed below.

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Respectfully submitted,


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